WHAT IS CLAIMED:

1. A DNA molecule encoding a recombinatorial substrate comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate;

a gene whose expression is to be controlled, said gene being positioned 3' to the promoter element to facilitate its transcription;

a terminator positioned 3' to said promoter and 5' to said gene whose expression is to be controlled to prevent transcription of genes 3' to said terminator; and

a first recombination site located 3' to said terminator and a second recombination site located 5' to said terminator, whereby treatment of said DNA molecule with a recombinase specific to said recombination sites removes said terminator from said DNA molecule, thereby activating the recombinatorial substrate and permitting transcription of said gene whose expression is to be controlled.

2. The DNA molecule of claim 1 further comprising:

a reporter gene located 3' to the terminator which facilitates the detection of an activated recombinatorial substrate either by producing an RNA or peptide which can be readily detected.

3. The DNA molecule of claim 2, wherein the reporter gene is selected from the group consisting of the genes encoding LacZ, chloramphenicol acetyl transferase, luciferase, the green fluorescent protein, human alkaline phosphatase, hygromycin resistance, and neomycin phospho-transferase.

4. The DNA molecule of claim 1 further comprising:

a 3′ flanking sequence which will stabilize the transcript and terminate transcription of said gene or said fragment located 3′ to the gene whose expression is to be controlled.

5. The DNA molecule of claim 4, wherein the 3′ flanking sequence is selected from the group consisting of a 3′ flanking region from a β-galactosidase gene, SV40, a β globin gene, a α-globin gene, and a human growth hormone gene.

6. The DNA molecule of claim 1, wherein said promoter element is selected from a group consisting of the promoters for the genes expressing: myosin heavy chain α, myosin heavy chain β, insulin, somatostatin, glucagon, growth associated protein 43 kDa, superior cervical ganglion clone 10, neurofilament-L, neurofilament-M, neurofilament-H, glial bifilary protein, P0, myelin associated glycoprotein, myelin basic protein, calcitonin-gene related peptide, and a neuron specific enolase.

7. The DNA molecule of claim 1, wherein said recombinase sites are selected from the group consisting of FRT, and loxP sites.

8. The DNA molecule of claim 1, wherein the terminator is selected from the group consisting of gastrin transcription terminator, C2 complement transcription terminator, and β-globin transcription terminator.

9. The DNA molecule of claim 1, wherein the gene whose expression is to be controlled is selected from the group consisting of a gene expressing a hormone, hormone receptor, neurotransmitter, neurotrophic factor, neurotrophic factor receptor, neuronal peptide, cell signaling molecule, and a receptor for any of the previously listed peptides.

10. The DNA molecule of claim 1, wherein the gene whose expression is to be controlled is a neuronal growth factor.

11. A vector containing the DNA molecule of claim 1.

12. A host cell carrying the DNA molecule of claim 1.

13. A transgenic mammal whose somatic and germ cells contain the DNA molecule of claim 1.

14. The transgenic mammal of claim 13, wherein the mammal is selected from the group consisting of a mouse, rat, goat, cow and pig.

15. A cell line, clone or tumor derived from the transgenic mammal of claim 13.

16. An embryonal stem cell clone containing the DNA molecule of claim 1.

17. A method of producing a transgenic mammal whose somatic and germ cells contain a recombinatorial substrate, comprising:

providing a recombinatorial substrate, comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate;

a gene whose expression is to be controlled, said gene being positioned 3′ to the promoter element to facilitate its transcription;

a terminator positioned 3′ and 5′ to said gene whose expression is to be controlled to said

promoter to prevent transcription of genes 3' to said terminator; and

a first recombination site located 3' to said terminator and a second recombination site located 5' to said terminator, whereby treatment of said DNA molecule with a recombinase specific to said recombination sites removes said terminator from said DNA molecule, thereby permitting transcription of said gene whose expression is to be controlled;

introducing the recombinatorial substrate into an embryo;

transplanting the embryo into a pseudopregnant mammal and allowing the transplanted embryo to develop to term; and

identifying a mammal which carries the recombinatorial substrate.

18. The method of claim 17, wherein said introducing is carried out by microinjection.

19. The method of claim 17, wherein said introducing is carried out by incorporating the recombinatorial substrate into a blastocyst of the embryo.

20. The method of claim 17, wherein said introducing is carried out by incorporating the recombinatorial substrate into embryonic stem cells.

21. The method of claim 17 further comprising:

interbreeding mammals carrying the recombinatorial substrate; and

identifying a progeny mammal which carries the recombinatorial substrate on two alleles.

22. The method of claim 17, wherein said identifying comprises identifying mammals which carry a reporter gene contained in the recombinatorial substrate.

23. The method of claim 22, wherein said identifying is carried out by detecting a protein expressed by the reporter gene.

24. The method of claim 22, wherein said identifying is carried out by screening for a phenotype conferred by the reporter gene.

25. The method of claim 22, wherein said identifying is carried out by hybridization to the reporter gene or an RNA molecule encoded by the reporter gene.

26. The method of claim 22, wherein the mammal is selected from the group consisting of a mouse, rat, goat, cow and pig.

27. A method of activating a gene to be expressed in a recombinatorial substrate, comprising:

providing a transgenic mammal carrying a recombinatorial substrate, comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate;

a gene whose expression is to be controlled, said gene being positioned 3′ to the terminator element to facilitate its transcription;

a terminator positioned 3′ to said promoter and 5′ to said gene whose expression is to be controlled to prevent transcription of genes 3′ to said terminator; and

a first recombination site located 3′ to said terminator and a second recombination site located 5′ to said terminator, whereby treatment of said

DNA molecule with a recombinase specific to said recombination sites removes said terminator from said DNA molecule, thereby activating the recombinatorial substrate and permitting transcription of said gene whose expression is to be controlled;

introducing into the transgenic mammal a recombinase which will promote the excision of DNA from said first recombination site to said second recombination site within the recombinatorial substrate; and

identifying a mammal which contains an activated recombinatorial substrate.

28. The method of claim 27, wherein said introducing comprises:

providing a vector which expresses the recombinase; and

introducing the vector into the cells of the transgenic mammal.

29. The method of claim 28, wherein the vector is a virus.

30. The method of claim 29, wherein the virus is selected from the group consisting of adenovirus, adeno-associated virus, lentivirus, vaccinia virus, sinbisvirus and retrovirus.

31. The method of claim 27, wherein said introducing is carried out by delivering a nucleic acid molecule which expresses recombinase into the cells of the transgenic mammal by use of virosomes, liposomes, naked DNA, or particle bombardment.

32. The method of claim 27, wherein the recombinase is selected from the group consisting of FLPs and *cre*.

33. The method of claim 27, wherein the mammal is selected from the group consisting of a mouse, rat, goat, cow and pig.

34. A DNA molecule encoding a recombinatorial substrate comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate;

a gene whose expression is to be controlled, said gene being positioned 3' to the promoter element to facilitate its transcription; and

a first recombination site located 3' to the gene whose expression is to be controlled and a second recombination site located 5' to the gene whose expression is to be controlled, whereby treatment of said DNA molecule with a recombinase specific to said recombination sites removes said gene whose expression is to be controlled from said DNA molecule, thereby activating the recombinatorial substrate and resulting in a loss of function of said gene whose expression is to be controlled.

35. The DNA molecule of claim 34 further comprising:

a terminator positioned 3' to said promoter to prevent transcription of genes 3' to said terminator and between said recombination sites; and

a reporter gene located 3' to the terminator and said recombinatorial sites to facilitate the detection of an activated recombinatorial substrate either by producing an RNA or peptide which can be readily detected.

36. The DNA molecule of claim 35, wherein the reporter gene is selected from the group consisting of the genes encoding LacZ, chloramphenicol acetyl transferase, luciferase, the green fluorescent protein, human alkaline phosphatase, hygromyciun resistance, and neomycin phospho-transferase.

37. The DNA molecule of claim 34 further comprising:

a 3' flanking sequence which will stabilize the transcript and terminate transcription of said gene or said fragment located 3' to the gene whose expression is to be controlled.

38. The DNA molecule of claim 37, wherein the 3' flanking sequence is selected from the group consisting of a 3' flanking region from a β-galactosidase gene, SV40, a β globin gene, a α-globin gene, and a human growth hormone gene.

39. The DNA molecule of claim 34, wherein said promoter element is selected from a group consisting of the promoters for the genes expressing: myosin heavy chain α, myosin heavy chain β, insulin, somatostatin, glucagon, growth associated protein 43 kDa, superior cervical ganglion clone 10, neurofilament-L, neurofilament-M, neurofilament-H, glial bifilary protein, P0, myelin associated glycoprotein, myelin basic protein, calcitonin-gene related peptide, and a neuron specific enolase.

40. The DNA molecule of claim 34, wherein said recombinase sites are selected from the group consisting of FRT and loxP sites.

41. The DNA molecule of claim 35, wherein the terminator is selected from the group consisting of gastrin transcription terminator, C2 complement transcription terminator, and β-globin transcription terminator.

42. The DNA molecule of claim 34, wherein the gene whose expression is to be controlled is selected from the group consisting of a gene expressing a hormone, hormone receptor, neurotransmitter, neurotrophic factor, neurotrophic factor receptor, neuronal peptide, cell

signaling molecule, and a receptor for any of the previously listed peptides.

43. The DNA molecule of claim 34, wherein the gene whose expression is to be controlled is a neuronal growth factor.

44. A vector containing the DNA molecule of claim 34.

45. A host cell carrying the DNA molecule of claim 34.

46. A transgenic mammal whose somatic and germ cells contain the DNA molecule of claim 34.

47. The transgenic mammal of claim 46, wherein the mammal is selected from the group consisting of a mouse, rat, goat, cow and pig.

48. A cell line, clone or tumor derived from the transgenic mammal of claim 46.

49. An embryonal stem cell clone containing the DNA molecule of claim 34.

50. A method of producing a transgenic mammal whose somatic and germ cells contain a recombinatorial substrate, comprising:

providing a recombinatorial substrate, comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate;

a gene whose expression is to be controlled, said gene being positioned 3' to the promoter element to facilitate its transcription; and

a first recombination site located 3' to the gene whose expression is to be controlled and a second recombination site located 5' to the gene whose expression is to be controlled, whereby treatment of said DNA molecule with a recombinase specific to said recombination sites removes said gene whose expression is to be controlled from said DNA molecule, thereby resulting in the loss of function of said gene whose expression is to be controlled;

introducing the recombinatorial substrate into an embryo;

transplanting the embryo into a pseudopregnant mammal and allowing the transplanted embryo to develop to term; and

identifying a mammal which carries the recombinatorial substrate.

51. The method of claim 50, wherein said introducing is carried out by microinjection.

52. The method of claim 50, wherein said introducing is carried out by incorporating the recombinatorial substrate into embryonic stem cells.

53. The method of claim 50, wherein said introducing is carried out by incorporating the recombinatorial substrate into a blastocyst of the embryo.

54. The method of claim 50 further comprising:

interbreeding mammals carrying the recombinatorial substrate; and

identifying a progeny mammal which carries the recombinatorial substrate on two alleles.

55. The method of claim 50, wherein said identifying comprises identifying mammals which carry a reporter gene contained in the recombinatorial substrate.

56. The method of claim 55, wherein said identifying is carried out by detecting a protein expressed by the reporter gene.

57. The method of claim 55, wherein said identifying is carried out by screening for a phenotype conferred by the reporter gene.

58. The method of claim 55, wherein said identifying is carried out by hybridization to the reporter gene or an RNA molecule encoded by the reporter gene.

59. The method of claim 50, wherein the mammal is selected from the group consisting of a mouse, rat, goat, cow and pig.

60. A method of activating a gene to be expressed in a recombinatorial substrate, comprising:

providing a transgenic mammal carrying a recombinatorial substrate, comprising:

a promoter element capable of promoting transcription of genes in the recombinatorial substrate;

a gene whose expression is to be controlled, said gene being positioned 3′ to the promoter element to facilitate its transcription; and

a first recombination site located 3′ to the gene whose expression is to be controlled and a second recombination site located 5′ to the gene whose expression is to be controlled, whereby treatment of said DNA molecule with a recombinase specific to said recombination sites removes said gene whose expression is to be controlled from said DNA molecule, thereby activating the

recombinatorial substrate and resulting in a loss of function of said gene whose expression is to be controlled;

introducing into the transgenic mammal a recombinase which will promote the excision of the DNA from said first recombination site to said second recombination site within the recombinatorial substrate; and

identifying a mammal which contains an activated recombinatorial substrate.

61. The method of claim 60, wherein said introducing comprises:

providing a vector which expresses the recombinase; and

introducing the vector into the cells of the transgenic mammal.

62. The method of claim 61, wherein the vector is a virus.

63. The method of claim 62, wherein the virus is selected from the group consisting of adenovirus, adeno-associated virus, lentivirus, vaccinia virus, sinbisvirus, and retrovirus.

64. The method of claim 60, wherein said introducing is carried out by delivering a nucleic acid molecule which expresses recombinase into the cells of the transgenic mammal by use of virosomes, liposomes, naked DNA and particle bombardment.

65. The method of claim 60, wherein the recombinase is selected from the group consisting of FLP and *cre*.

66. The method of claim 60, wherein the mammal is selected from the group consisting of a mouse, rat, goat, cow and pig.